REMARKS

In the Office Action, Claims 19-31 have been withdrawn from consideration; Claims 2-8 are rejected under 35 U.S.C. § 112, second paragraph; and Claims 2 and 3 are rejected under 35 U.S.C. § 103. Claim 2 has been amended. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Versions with Markings to Show Changes Made**." Applicants respectfully submit that the rejections have been overcome or are improper in view of the amendments and/or for the reasons set forth below.

At the outset, the Examiner has withdrawn Claims 19-31 that were newly submitted in Applicants' Response to Restriction Requirement mailed on December 12, 2001. Applicants believe that the withdrawal of Claims 19-31 from consideration is improper. Of course, "if the search and examination of the entire application can be made without serious burden, the Examiner must examine on the merits, even though it includes claims of independent and distinct inventions". See, MPEP § 803.

Even if the inventions embodied by Claims 2-8 and 19-31 are distinct inventions pursuant to the MPEP, Applicants do not believe that the scope of the claimed subject matter is so greatly different that it would impose a serious burden on the Examiner to examine Claims 2-8 and Claims 19-31, together, on the merits. At the outset, Applicants question why the Examiner considers Claim 19 not to include two different solutions. Indeed, Claim 19 recites a first part of a peritoneal dialysis solution that includes dextrose and a second part of the peritoneal dialysis solution that includes polypeptides wherein either of a first or a second structure houses the first and second part, respectively, and includes a sufficient amount of ingredients so when the first part and the second part are mixed, a range of concentration of ingredients results as recited in Claim 19.

Further, Applicants do not believe that the additional pH and dextrose features as required by Claims 2-8 in comparison to Claims 19-31 are so substantial that the differences would impose a serious burden on the Examiner to search and examine, on the merits, Claims 2-8 together with Claims 19-31. Indeed, the subject matter of Claims 2-8 and Claims 19-31 each relate to a two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient. Therefore, Applicants respectfully request that Claims 19-31 be examined on the merits together with Claims 2-8.

In the Office Action, Claims 2-8 are rejected under 35 U.S.C. § 112, second paragraph. With respect to Claim 2, the Examiner asserts that it is not clear what the term "including" refers to. As previously discussed, Applicants have amended Claim 2. More specifically, in line 2 of Claim 2, the term "the first part" has been added to clarify that the term "including" refers to the first part. In addition, a similar change was made to line 3 of Claim 2 where the term "the second part" was added to clarify that the term "including" in this part of Claim 2 refers to the second part.

With respect to the use of the claim terms "approximately" and "about," Applicants do not believe that the use of such terms render the scope of the claimed subject matter unclear. The Specification clearly supports these claim terms. See, for example, page 7, lines 1-10. Further, the use of descriptive claim terms, such as "approximately" and "about" are not generally considered to render the claims indefinite. In this regard, Applicants believe that one skilled in the art would clearly understand the scope and meaning of the claimed invention as required by Claims 2-8. Therefore, Applicants believe that Claims 2-8 fully comply with 35 U.S.C. § 112.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

In the Office Action, Claims 2 and 3 are rejected under 35 U.S.C. § 103. More specifically, Claim 2 is rejected as being unpatentable over U.S. Patent No. 4,880,629 ("*Okamoto*") in view of U.S. Patent No. 5,039,609 ("*Klein*"); and Claims 2 and 3 are rejected as being unpatentable over *Klein* in view of U.S. Patent No. 5,011,826 ("*Steudle*").

Applicants believe that the obviousness rejections are improper. Of the rejected claims, Claim 2 is the sole independent claim. Claim 2 recites a two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient. The two part peritoneal dialysis solution includes, in part, a first part housed in a first structure and a second part housed in a second structure. The first part includes approximately 1.0 to about 8% (w/v) dextrose and a pH of approximately 4.0 to about 5.5; and the second part includes approximately 0.5 to about 8.0% (w/v) polypeptides and a pH of approximately 6.0 to about 7.5.

The present invention provides an improved dialysis solution. The improved dialysis solution provides for the use of specific polypeptides as an osmotic agent with an additional osmotic agent, such as dextrose. The inventors have found that selecting well defined polypeptides and utilizing same with an additional osmotic agent can overcome the

disadvantages of using polypeptides alone or dextrose alone set forth on pages 10-26 of the Specification.

For example, the test Example 1 was conducted to evaluate the peptides disclosed in European Patent No. 0218900 (equivalent to *Klein*) as alternative osmotic agents to dextrose in dialysate solutions. Example 2 sets forth irritation screening that was conducted on a variety of solutions. Applicants believe that the experiments clearly demonstrate advantages of the present invention. In this regard, the above examples (Example Nos. 1 and 2) demonstrate that the use of only a polypeptide mixture, such as that set forth in *Klein*, is not clinically acceptable in a peritoneal dialysis solution.

In order for the polypeptide composition of *Klein* to obtain the absorption equivalent to a 2.5% dextrose solution, one needs at least a 5.5% polypeptide solution. However, Example No. 1 demonstrates that the absorption of the polypeptide is at least 50% to 60%. If polypeptides, at an at least 5% concentration in a dialysis solution are used at every exchange, the patient would receive at least 200 grams of amino acids per day. It has been found that peritoneal absorption of more than 40 grams of amino acids per 24 hours can cause uremia in dialysis patients.

Accordingly, due to the absorption characteristics of the polypeptides, it has been determined that preferably only a 1% to 2% concentration of a polypeptide solution, such as *Klein*, should be used. However, at such a concentration, the polypeptides do not provide a sufficient osmotic agent. It has also been found that in order to control uremia problems, it is necessary to control the proportion of lower molecular weight peptides.

Example No. 2 demonstrates that the polypeptides of *Klein* have the potential for immunogenicity. The problem stems from the fact that too great a proportion of peptides in *Klein* have a molecular weight above 1200. It has been found that not more than 0.10% of the polypeptides should have a molecular weight of greater than 1,200.

Accordingly, pursuant to the present invention, the polypeptides are used in a specific concentration of, for example, about 1% to about 8% with an osmotic agent, such as dextrose in a concentration of 0.5% to 8%. Further, the polypeptides of the claimed invention can have an average molecular weight of about 400 to about 900 daltons.

This can minimize the risk of immunogenic response. Additionally, not more than 25% of the polypeptides should have a molecular weight of less than 400. This prevents the uremic problems that will occur with the solution proposed in *Klein*. Further, the polypeptide solutions

of *Klein* have the potential of producing allergic reactions, due to the size of the polypeptides used in solution. In contrast, the claimed polypeptides have a size that will not produce such allergic reactions. Therefore, Applicants believe that the two part peritoneal dialysis solutions of the claimed invention requires a specific composition including specific amounts of polypeptides and dextrose that can be used in peritoneal dialysis to overcome the disadvantages of *Klein*.

Even if combinable, Applicants do not believe that the other cited references, namely, *Okamoto* and *Steudle*, can remedy the deficiencies of *Klein*. In this regard, the Examiner merely relies on *Okamoto* for its alleged teaching regarding the use of glucose in a peritoneal dialysis solution.

Contrary to the Examiner's assertion, nowhere does *Klein* or *Okamoto* provide the sufficient motivation to combine the alleged teachings of *Klein* and *Okamoto* with respect to a solution containing glucose and peptides and/or separate solutions of glucose and peptides for "sequential use" during dialysis. *Okamoto* merely relates to dialytic solutions that contain glycerol and monosaccharides as osmotic pressure regulating agents for regulating the osmotic pressure necessary for the removal of water. See, *Okamoto*, col. 5, lines 15-20. Further, the Examiner's attempt to suggest that *Klein* provides such motivation is a clear mischaracterization of *Klein*. Indeed, the purpose of *Klein* is to provide peritoneal dialysis solutions which include peptides as a substitute to glucose. See, *Klein*, Background of the Invention.

Moreover, the Examiner suggests that Claim 2 does not require that the two solutions be used on the same patient, or that their use be recommended by the same physician. Applicants respectfully submit that the Examiner has confused the scope and meaning of the subject matter of Claim 2. Indeed, Claim 2 recites, in part, a two part peritoneal dialysis solution designed to be **mixed** prior to infusion into **a patient**. Therefore, Applicants believe that *Okamoto* and *Klein*, even if combinable, fail to disclose or suggest a number of features of the claimed invention.

With respect to the alleged teaching of *Steudle*, Applicants respectfully submit that the mere mention of a combination of peptide with glucose in the same sentence is not sufficient grounds for an obviousness rejection contrary to the Examiner's position. See, *Steudle*, col. 4, lines 51-59. Moreover, *Steudle* does not remedy the deficiencies of *Klein* with respect to the polypeptide features of the claimed invention. *Steudle* does not even provide any description of peptides that can be used as osmotic agents.

Indeed, *Steudle* does not define the circumstances wherein one would mix peptides with an osmotic agent, such as dextrose as required by the claimed invention. Instead, *Steudle* merely relates to the use of galactose as an osmotic active substance. In attempting to provide as broad a disclosure as possible, the *Steudle* patent makes a backhanded reference to peptides in column 4, line 58, along with an exhaustive list of the groups of possible osmotic agents to be used in addition to galactose and glucose. Therefore, Applicants do not believe that one skilled in the art would be inclined to modify *Klein* in view of same to arrive at the claimed invention.

At best, the cited art, even if combinable, simply provides "general guidance" as to the particular form of the claimed invention. Absent a suggestion, teaching or motivation of the specific compositions of the two part peritoneal dialysis solutions including polypeptides and dextrose claimed in the present invention, Applicants respectfully submit that the Examiner has impermissibly applied hindsight reasoning in support of the prior art rejections.

Based on the apparent differences between the cited art and the claimed invention, Applicants believe that the cited art fails to disclose or suggest a number of features of the claimed invention. Therefore, Applicants respectfully submit that the cited art, even if combinable, fails to render obvious the claimed invention.

Accordingly, Applicants respectfully request that the obviousness rejections with respect to the claimed invention be withdrawn.

Applicants note for the record, that the Examiner has refused to consider a number of references cited in the Information Disclosure Statement ("IDS") submitted by Applicants on September 26, 2001. With respect to U.S. Patent Nos. 4,168,337 ("'337") and 3,939,261 ("'261"), Applicants believe that the Examiner's refusal to consider these references is improper. In this regard, each of these references were identified in the previously submitted IDS, in addition to a copy of same. With respect to the '337 patent, the named inventor is Maistre and the issue date is September 18, 1979. Applicants are submitting a Supplemental Information Disclosure Statement concurrently with this Response to indicate the correct Inventor Name and Issue Date for the '337 patent. Further, Applicants believe that the Supplemental Information Disclosure Statement should resolve the issues with respect to the remaining references that the Examiner has refused to consider.

Accordingly, Applicants respectfully request that the Examiner consider all the references at issue and further request that an initialed PTO Form 1449 acknowledging same be returned to Applicants.

For the foregoing reasons, Applicants respectfully request reconsideration of their patent application and earnestly solicit an early allowance of same.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

2. (Amended) A two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient comprising:

a first part housed in a first structure, the first part including approximately 1.0 to about 8% (w/v) dextrose and a pH of approximately 4.0 to about 5.5;

a second part housed in a second structure, the second part including approximately 0.5 to about 8.0% (w/v) polypeptides and a pH of approximately 6.0 to about 7.5; and

including in either the first or the second structure a sufficient amount of the following ingredients so when the first part and second part are mixed, the following is provided: 120 to about 150 (mEq/L) sodium; 80.0 to about 110.0 (mEq/L) chloride; 0.0 to about 5.0 (mEq/L) lactate; 0.0 to about 45.0 (mEq/L) bicarbonate; 0.0 to about 4.0 (mEq/L) calcium; and 0.0 to about 4.0 (mEq/L) magnesium.